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| FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624 | | | LIN, JERRY | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1631 | |

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/773,032

Applicant(s)

LEE ET AL.

Examiner

Jerry Lin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 13, 16, 19-21, 23, 24, 26-28, 30-34 and 42-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 13, 16, 19-21, 23, 24, 26-28, 30-34, 42-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3 pages.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments and amendments, filed March 29, 2006, have been fully considered and they are deemed to be persuasive. Rejections from previous office actions are hereby withdrawn. However, the following rejections are newly applied as necessitated by amendment. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-9, 13, 16, 19-21, 23, 24, 26-28, 30-34, and 42-47 are under examination.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9, 13, 16, 19-21, 23, 24, 26-28, 30-34, 42-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 1 and 2 recites the term "selectively interact". It unclear if "selectively interact" means that the capture agents will only bind to a peptide tag of a target protein, or if the capture agents will have some other affinity to a few different peptide tags.

5. Claim 16 recited that for each capture agent the method has a regression coefficient of 0.95 or greater. It is unclear for what the regression coefficient is being

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calculated. One interpretation is that is calculated for binding. Another interpretation is that it is calculated for affinity.

6. Claims 30 and 42 recite the term "splice variant proteins." A review of the literature has revealed that the concept of "splice variants" refers to nucleic acids, specifically RNA. "Splice variants" do not refer to proteins. It is unclear if the term "splice variant proteins" refers to proteins that are produced from splice variant RNA or if the term refers to proteins that have been spliced (i.e., fragmented, cleaved, etc.). For purposes of this office action, the latter interpretation will be used.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 30-34, 42, 44, and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Katz (US 2002/0137119 A1).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents.

In addition, the examiner is interpreting peptide epitope tags as epitopes that are found on peptides, since there is no explicit definition of the term in the specification.

Regarding claims 30, 34, 42, 44, and 46, Katz teaches a method of fragmenting proteins using a predetermined denaturation and proteolytic protocol to generate a solution of polypeptide analytes comprising peptide epitope tags that indicate the presence of the sample of the protein (page 8, paragraphs 0136-0147); providing an addressable array of capture agents that can interact with the peptide epitope tag (page 8, paragraphs 0139-0140); contacting the array to the solution (page 8, paragraph 0141).

Regarding claim 31, Katz teaches that the solid support may be beads or an array device with features that encode the identify of the capture agents (page 8, paragraph 0140; page 14, paragraph 0191).

Regarding claim 32, Katz teaches where there are 2-100 capture agents (page 14, paragraph 0191).

Regarding claim 33, Katz teaches using a single chain antibody (page 7, paragraph 0127).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 3-5, 7-9, 19, 21, 24, 28, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katz (US 2002/0137119 A1) in view of Suzuki et al. (US 5,955,317).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents, and using a secondary capture agent labeled with a detectable moiety to detect a captured fragment.

In addition, the examiner is interpreting peptide epitope tags as epitopes that are found on peptides, since there is no explicit definition of the term in the specification.

Regarding claim 1, Katz teaches a method of fragmenting proteins using a predetermined denaturation and proteolytic protocol to generate a solution of polypeptide analytes comprising peptide epitope tags that indicate the presence of the sample of the protein (page 8, paragraphs 0136-0147); providing an addressable array

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of capture agents that can interact with the peptide epitope tag (page 8, paragraphs 0139-0140); contacting the array to the solution (page 8, paragraph 0141).

Although Katz teaches that a variety of detection methods may be used, Katz does not specifically teach using a secondary capture agent to detect analytes.

Regarding claim 1 and 5, Suzuki et al. teaches using a sandwich assay where the secondary capture agents are specific for a captured polypeptide and labeled with a detectable moiety (column 3, line 40- column 3, line 20; column 8, lines 3-19).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Katz with Suzuki et al. to gain the advantage of being able to detect a biomarker for Alzheimer's disease. Katz teaches a general method of detecting proteins in a sample. Katz states that her method may be used for diagnosing a variety of disease including Alzheimer's disease (page 9, paragraph 0132). Thus one of ordinary skill in the art using Katz's method would seek out antibodies that are highly specific for biomarkers of Alzheimer's disease. Suzuki et al. disclose an antibody that is highly specific for a biomarker of Alzheimer's disease (column 3, lines 1-15). Thus one of ordinary skill in the art, seeking to diagnose Alzheimer's disease, would be motivated use the antibodies disclosed in Suzuki et al.'s method with an array from Katz.

Regarding claims 3 and 4, Katz teaches where the capture agents are antibodies or nonantibody polypeptides (page 8, paragraph 0139, 0147).

Regarding claims 7-9, Katz teaches creating a biopsy digest (page 14, paragraphs 0187-0189) which would contain multiple forms of protein such as pro-form or mature form proteins, and splicing forms.

Regarding claim 19, Katz teaches a variety of sample sources (page 8, paragraph 0136).

Regarding claim 21, Katz teaches treating membrane bound proteins (page 13, paragraph 0178)

Regarding claim 24, Katz teaches where the label may be a fluorophore (page 8, paragraph 0142).

Regarding claim 28, Katz teaches where the target proteins may serve as a biomarker (page 8, paragraph 0132).

Regarding claim 42, Katz is applied as above.

Regarding claim 43, Suzuki et al. teaches using a sandwich assay where the secondary capture agents are specific for a captured polypeptide and labeled with a detectable moiety (column 3, line 40- column 3, line 20; column 8, lines 3-19).

12. Claims 2, 6, 13, 23, 26, 27, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katz (US 2002/0137119 A1) in view of Suzuki et al. (US 5,955,317) in view of Wagner et al. (US 6,897,073 B2).

Katz and Suzuki et al. are applied as above.

However, Katz does not teach determining the amount of target protein in the sample by averaging the results obtained from each said capture agent.

Regarding claims 2, 20, 21, and 45, Wagner et al. also teach a method of detecting proteins using arrays of protein-capture agents (abstract) which includes contacting the array with cleaved or denatured protein analytes (membrane bound proteins) from body fluids (column 35, lines 22-44) and quantifying the amount of a target protein by averaging the result (including if the total amount of the detected proteins is averaged by one spot in the array) (column 35, line 63-column 36, line 23; column 39, lines 12-50).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods from Katz, Suzuki et al. and Wagner et al. to gain the advantage of creating arrays that can process multiple proteins. The motivation to combine Katz with Suzuki et al. is applied as above. Although Katz and Suzuki et al. teach using arrays of antibodies, Wagner et al. has the added benefit of detecting and quantifying multiple proteins. Thus one of ordinary skill in the art seeking to detect and quantify a large number of proteins in a sample, for example several biomarkers of Alzheimer's disease, would be motivated to utilize Wagner et al.'s teachings with Katz and Suzuki et al.

Regarding claim 6, Wagner et al. teach arrays with capture agents bind to the same PET (column 12, line 14 - column 13, line 30).

Regarding claims 7-9, Wagner et al. teach using cellular extracts which would contain multiple forms of protein such as pro-form or mature form proteins, and splicing forms (column 35, lines 22-44).

Regarding claims 13, Wagner et al. teach detecting protein fragments (processed forms) of cellular extracts and determining the ratio of one form of protein to another form (column 45, lines 32-39; column 38, lines 43-65).

Regarding claim 23, Wagner et al. teach wherein a secondary capture agent may be used for detection using fluorescent methods (column 36, lines 24-57).

Regarding claim 26, Katz teaches wherein the sample contains billion molar excess of unrelated proteins or fragments (page 13, paragraphs 0178-0183).

Regarding claim 27, Wagner et al. teach wherein the PET is identified based on a sequenced genome (column 30, lines 42-54).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

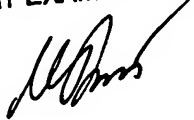
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MICHAEL BORIN, PH.D
PRIMARY EXAMINER



JL